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Late-breaking abstracts

TITLE: GSK-3β blockade with 9-ING-41 in melanoma: The 1801 Phase 1/2 study

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Background: GSK-3β is a serine/threonine kinase that regulates tumor progression, oncogenesis, cell cycle and epithelial-mesenchymal transition. Overexpression of GSK-3β is associated with advanced stage, aggressive growth and chemotherapy resistance. GSK-3β inhibition reduced proliferation and induced apoptosis of melanoma cell lines (Kubic Mol Can Res 2012). These data provided the rationale for inclusion of patients with melanoma in a Phase 1/2 study evaluating the small molecule, first-in-class GSK-3β inhibitor 9-ING-41.
Methods: Part 1 of the 1801 study evaluate safety, and delineate the recommended Phase 2 study dose for 9-ING-41 monotherapy in patients with refractory malignancies. Patients receive twice-weekly intravenous infusions of 9-ING-41 until toxicity or progression. Response is defined by RANO criteria for brain metastases and RECIST 1.1 for other masses in evaluable lesions.The study is open in 25 sites globally and will accrue about 300 patients.
Results: To date, 3 patients with melanoma were accrued among a total of 70 patients. Five dose levels (1, 2, 3.3, 5, 7 mg/kg) have been completed without 9- ING-41 attributable SAE. A complete radiologic including brain metastases response was observed at 12-week assessment and confirmed on scans at 18 and 24 weeks from initiation of 9-ING-41 (5 mg/kg) monotherapy in one patient with BRAF V600K mutated metastatic melanoma refractory to nivolumab/ipilimumab sequenced with dabrafenib/trametinib. Another patient had stable disease on 6-week scan and a third patient completed one month of therapy. Grade 1 transient color perception changes attributed to 9-ING-41 was observed in 38% (17/45) of patients.
Conclusion: A complete response lasting 12 weeks to date was observed in a patient with refractory metastatic melanoma on 9-ING-41. The compound is well tolerated with stable predictable PK. Accrual of patients with advanced melanoma is ongoing.